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Endocrine disrupters and human health

Current research will establish baseline indices

Infertility is an emotive issue, and having children is a recognised "right," so any implication that environmental pollution affects reproduction has to be taken seriously. When the putative causative agents might also be responsible for various cancers and other diseases, then the level of interest that the issue attracts is unsurprising—hence the calls in the early 1990s for action in line with the "precautionary principle."[1] In men hypospadias, cryptorchidism, cancer of the prostate, testicular cancer, and semen quality and in women breast cancer, cystic ovaries, and endometriosis have all been suggested as indicators of adverse trends in reproductive health.[2] The idea that these trends are real and are connected with environmental pollution is gaining credence internationally. The effect on human health of environmental chemicals that are mediated through the endocrine system—endocrine disrupters—has generated huge interest and investment. Why is this, and what is the evidence for the assumed association?

Changes in the sexual morphology of fish exposed to sewage effluent have led some scientists to conjecture that humans also live in a "sea of oestrogens" and that the apparent increases in the incidence of certain reproductive conditions may be due to exposure to chemicals in the environment. The so called Sharpe-Skakkebaek hypothesis offered a possible common cause and toxicological mechanism for abnormalities in men and boys—that is, increased exposure to oestrogen in utero may interfere with the multiplication of fetal Sertoli cells, resulting in hormonally mediated developmental effects and, after puberty, reduced quality of semen.[3] It was postulated that synthetic chemicals in the environment are the prime source of the excessive oestrogenic stimulation, with exposure through food and water being the primary route. Further research has extended the concern to the role of antiandrogens and has led to the recognition that a range of systems and processes may be susceptible to hormonal modulation, including immune function, behaviour, and learning and memory, as well as reproduction. The term environmental oestrogen has given way to the more encompassing term "environmental endocrine disrupter," defined as "an exogenous substance that causes adverse health effects in an intact organism, or its progeny, subsequent to changes in endocrine function."[4]

Endocrine disrupters are potentially present in food as natural "phytoestrogens" and chemical contaminants, and there is a divide in the perception of natural and synthetic substances.[5] Hence the drive in some quarters to market "healthy" bread that is rich in soya flour and linseed at the same time that other people are warning against low levels of weak oestrogenic synthetic chemicals as contaminants in food. Perhaps this reflects the common view of natural things as good and synthetic things as necessarily bad.

Two questions need to be addressed. Do indicators of reproductive health truly reveal a worsening situation? Can exposure to environmental chemical contaminants conceivably be the cause of any such temporal changes? Baseline data on many of the implicated conditions are so poor that it is not possible to say for sure whether trends are occurring. There is also the issue of geographical variability in the measured indices, which can be related to genetic differences in the population or to climatic differences or changes in lifestyle, for example. None the less, there is agreement that the incidence of testicular and prostate cancer is increasing and that semen quality is probably worsening in some regions of the world. There is also some evidence for an increasing incidence of cryptorchidism and hypospadias; and in women endometriosis and polycystic ovaries may be more common.[4–6]

Perhaps the most controversial issues in research on endocrine disrupters are the possible disproportionate effects of low levels of exposure, as proposed by Vom Saal et al and recently accepted by the US national toxicology programme, at least for a limited number of chemicals[7–9]; the question of synergism in mixtures, which has become something of a no go area since the withdrawal of the much quoted paper by Arnold et al[10]; and the development of appropriate test methods. Large amounts of resources have been invested in this last activity, through the work of the endocrine disrupter screening and testing advisory committee in the United States. Yet according to Ashby the developmental effects of endocrine disruptors that are seen in rodent studies cannot be extrapolated to humans. This is not only because of the uncertainty of applying such results across species but also because of the absence of an agreed control database in rodents and the variability in test protocols and in the developmental effects in test animals.[11]

Among specific chemicals implicated as endocrine disrupters phthalates may be of particular importance because of their ubiquity. Similarly bisphenol A has been shown in both in vitro and in vivo assays to have high potential for endocrine disruption and potential for exposure to humans—for example, through its use

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in can linings. These are issues of major interest, not least because of the possible exposure of infants to these chemicals at critical stages of development. Sharpe has argued that, until appropriate in vivo experiments are done, phthalates and similar chemicals will continue to cause concern for testicular development.[12] Meanwhile the debate about phytoestrogens and women's health continues: on the one hand there is concern that any hormonally active substance can induce or exacerbate breast and uterine cancer, and on the other is the knowledge that these substances can be used as alternatives to hormone replacement therapy in the treatment of postmenopausal symptoms and osteoporosis.[13]

This is a fascinating area with important repercussions, and it is appropriate to investigate environmental causes of disease. Research is now being undertaken that will establish baselines for some key indices of reproductive health, which should allow future researchers to resolve the current uncertainties and determine the impact of endocrine disrupters on our health.

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Estimating the financial requirements of health care

The Wanless report is a pioneering effort—with a few omissions and errors

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Seemingly on the edge of financial shipwreck not so long ago, the National Health Service is now sailing on a springtide of money, promises, and hope. Mr Gordon Brown, chancellor of the exchequer, has added an extra billion pounds to swell an already unprecedented rate increase in the NHS's budget. Mr Tony Blair, prime minister, has reiterated the British government's commitment to achieving the average level of spending in the European Union. The great unmentionable, tax increases to fund the NHS's growth, has appeared on the agenda of political debate.

So why are the corridors of the NHS not ringing with the hosannas of grateful staff and patients? One reason is scepticism about the government's ability to deliver. Achieving the government's spending target depends on Britain not becoming a casualty of a global economic recession. Moreover, uncertainty is compounded by controversy about just how many more billions will be needed to achieve the target.

But there is a more fundamental reason for not being swept away by the government's pledges. This is that the target itself is a nonsense (interestingly, Mr Blair has himself watered down the commitment (p 1325)). The European Union average of spending on health care is a statistical artefact. In 1998 spending on health care in the union ranged from 6.8% of the gross domestic product in Ireland (much the same as in the United Kingdom) to 10.3% in Germany.[1] It is not self evident that averaging this out—whether on an income weighted basis (8.4%) or on an unweighted basis (7.9%)—provides any kind of guide to what the United Kingdom's level of spending should be.

Hence the importance of Mr Derek Wanless, former chief executive of NatWest Bank, charged by the chancellor of the exchequer to estimate the resources required to run the health service in 20 years time. His interim report attracted much attention for the wrong reason.[2] It appeared to rule out alternatives to general taxation as a method of funding health, an interpretation subsequently repudiated by Mr Wanless. In fact, the Wanless review, as the interim report explicitly recognises, was "not set up to examine the way in which those resources are financed." And its analysis of different methods of funding is a dutiful review of familiar arguments, with the occasional error thrown in. For example, it makes the patently wrong claim that "there is little scope for expression of individual choice under social insurance models." Given that the review's advisory group is made up entirely of officials, nothing else could perhaps be expected. The review's final report could usefully concentrate on its main task, estimating future financial requirements.

This task is challenging enough. The interim report sets out the questions to be asked, discusses the methodological problems involved, and invites comments on both. Inevitably it is more successful in identifying the factors likely to drive demands—demographic changes, technological developments, and rising public expectations—than quantifying their impact. Some specific conclusions do emerge. The effects of an ageing population are likely to be relatively modest. The costs of policy initiatives designed to bring NHS services up to European levels of excellence—as embodied in national service frameworks—can be costed, and are not likely to

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